Do the Codes Apply to My Research? Nuremberg, Helsinki, the Belmont Report, CIOMS, and the Common Rule

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Research Ethics Codes

- Nuremberg Code (1947)
- Declaration of Helsinki (1964/2008)
- The Belmont Report (1979)
- Council for International Organizations of Medical Sciences (CIOMS (1982/2002)
- The Common Rule (45 CFR Part 46, Subpart A, 1974/1991)

MORE Research Ethics Codes

- 45 CFR Part 46 Subparts B, C, D
- 21 CFR Parts 50, 56, 312, 812 (FDA)
- HIPAA, FERPA, PPRA, CIPSEA,
- ICH E6 GCP
- Maryland State Law: House Bill 917 “Human Subject Research - Institutional Review Boards”, (and New York, California, etc….)

AND MORE Research Ethics Codes

- Hippocratic Oath (5th Century BCE)
- American Medical Association (2001)
- American Nursing Association (2001)
- American Psychological Association (2010)
- American Education Research Association (2011)
- See: OHRP International Compilation at http://www.hhs.gov/ohrp/international/intlcompilation/intlcompilation.html

Nuremberg Code

- “The voluntary consent of the human subject is absolutely essential.”
- Investigator responsibility
- Fruitful results
- Avoid suffering and injury
- Subject or Investigator may discontinue

Declaration of Helsinki (2008)

- "…the well-being of the individual research subject must take precedence over all other interests."
- Some subjects are incapable of consent.
- Placebo trials are ethical *sometimes*.
- Prospective committee approval is required.
- Under-represented populations should have access to participation.
- Vulnerable populations who participate should also benefit.

CIOMS

- Applies the Declaration of Helsinki to research in under-developed/low resource countries.
- Scientific and ethical review are inseparable.
- Investigators must insure subject's understanding.
- Risks to groups should be considered.

CIOMS (cont.)

- Other vulnerable groups: "…medical and nursing students, subordinate hospital and laboratory personnel, employees of pharmaceutical companies, and members of the armed forces or police…"
- "In research involving women of reproductive age....only the informed consent of the woman herself is required for her participation. In no case should the permission of a spouse or partner replace the requirement of individual informed consent."

CIOMS (cont.2)

- Developed interventions should be made available to community where research occurs.
- Beneficial drugs should be provided to subjects post-study.
- Subjects injured in research are entitled to treatment and financial compensation.
- Research infrastructure capacity in developing countries should be strengthened.

The Belmont Report

- Advancement of the socially valued practice of research
- Boundary between research and practice
- Respect for Persons/Informed Consent (& Protection of Limited Autonomy)
- Beneficence/Assessment of Risks and Benefits
- Justice/Selection of Subjects

Mechanisms of the Common Rule

- "…this policy applies to all research involving human subjects conducted, supported or otherwise subject to regulation…"[.101(a)]
- [including]:
  - An Assurance of compliance
  - Institutional Review Board (IRB) review and approval
  - Informed Consent of the Subject

Informed Consent in the Common Rule

- Informed Consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 46.116. (.111(a)(4))
- .116 requires:
  - Sufficient opportunity to consider participation
  - Minimization of coercion or undue influence
  - Information in understandable language
- .116 allows waiver of informed consent in some circumstances

Beneficence in the Common Rule

- Risks to subjects are minimized: (1) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk,…(111(a)(1))
- Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result….(111.(a)(2))

Justice in the Common Rule

- Selection of Subjects is equitable….the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons. (111(a)(3))

What does “Apply” mean?

The Challenge of Applying Codes

- “The codes consist of rules, some general, others specific, that guide the investigators or the reviewers of research in their work. Such rules often are inadequate to cover complex situations; at times they come into conflict, and they are frequently difficult to interpret or apply. Broader ethical principles will provide a basis on which specific rules may be formulated, criticized and interpreted.” (Belmont)

The Challenge of Applying Principles

"Three principles, or general prescriptive judgments, that are relevant to research involving human subjects are identified in this statement…. Other principles may also be relevant. These principles cannot always be applied so as to resolve beyond dispute particular ethical problems. The objective is to provide an analytical framework that will guide the resolution of ethical problems arising from research involving human subjects." (Belmont)

Why Does It Matter if a Code Applies?

Do I have to follow the Code? (E.g.)

1. I am the Lord your God; You shall have no other gods before me.
2. You shall not make for yourself an idol.
3. Do not take the name of the Lord in vain.
4. Remember the Sabbath and keep it holy.
5. Honor your father and your mother.
6. You shall not kill/murder.
7. You shall not commit adultery.
8. You shall not steal.
9. You shall not bear false witness against your neighbor.
10. You shall not covet your neighbor's wife.
11. You shall not covet anything that belongs to your neighbor.

Kohlberg's 6 Stages of Moral Development

1. Obedience and punishment orientation
2. Self-interest orientation
3. Interpersonal accord and conformity
4. Authority and social-order maintaining orientation
5. Social contract orientation
6. Universal ethical principles

Why Should I Follow the Code?

- Nuremberg Code
- Declaration of Helsinki
- The Belmont Report
- CIOMS
- The Common Rule (45 CFR Part 46, Subpart A)

Why do I follow the Code?

- Do codes work?
- What else works?

Could I revise the code?

"Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay and Ambiguity for Investigators"

(Advance Notice of Proposed Rulemaking (ANPRM), Federal Register July 26, 2011)

ANPRM Proposals

- Scope of regulatory jurisdiction
- Revised tiers of review
- Single IRB review for domestic multi-site studies
- Informed Consent improvements
- Single set of security/confidentiality standards
- Biospecimen research
- Data Reporting
- Uniformity of regulatory guidance

ANPRM Comments due 10/26/11

Identify by docket ID number HHS-OPHS-2011-0005

- Federal eRulemaking Portal: http://www.regulations.gov/
- Mail/Hand delivery/Courier [For paper, disk, or CD-ROM submissions] to: Jerry Menikoff, M.D., J.D., OHRP, 1101 Wootton Parkway, Suite 200, Rockville, MD 20852.

Comments received, including any personal information, will be posted without change to http://www.regulations.gov/